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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/117,218	01/11/1999	SUSANNE M. BROWN	117-261	3436

7590 12/10/2004

Klarquist Sparkman Campbell Leigh & Whinston, LLP
One World Trade Center
Suite 1600
Portland, OR 97204

EXAMINER	
NGUYEN, QUANG	
ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 12/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/117,218	BROWN ET AL.	
	Examiner	Art Unit	
	Quang Nguyen, Ph.D.	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 September 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *33 and 37-40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *33 and 37-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 33 and 37-40 are pending in the present application, and they are examined on the merits herein.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 33 and 37-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Roizman et al. (U.S. Patent No. 6,340,673; Cited previously) in view of Randazzo et al. (Virology 211:94-101, 1995; IDS) for the same reasons already set forth in the Office Action mailed on 6/23/04 (pages 2-5).

Response to Arguments

Applicant's arguments related to the above rejection in the Amendment filed on 9/27/04 (pages 2-6) have been fully considered, but they are respectfully not found persuasive.

With respect to the Randazzo paper, Applicants argue that from the paper an ordinary skilled artisan would conclude that 1716 is effective to lyse many, but not all, melanoma cell types *in vitro*, with no information as to selectivity. Additionally, the *in vivo* data in the paper all relate to intracranial tumor, wherein it is recognized that the tumor is an isolated dividing cell population amongst a brain tissue consisting of non-dividing cells, and that the paper does not teach that 1716 is selective in itself for lysis of tumor cells whilst not lysing non-tumor dividing cells. With respect to the US Patent 6,340,673 (Roizman), Applicants mainly argue that the issued patent only discusses primary neuronal tumors, and does not teach the treatment of a non-neuronal tumor, or the use of the specific virus HSV-1 1716. Applicants further argue that there is no reasonable expectation of success for combining the teachings of the Randazzo paper with US Patent 6,340,673 because applying the teaching of Randazzo to the skin, an example of non-neuronal tissue type, one might expect HSV-1 1716 to result in lysis of tumor cells (melanoma cells) but one would also expect lysis of healthy non-tumor dividing cells to occur. Therefore, this would not provide a safe and effective treatment in that the healthy dividing cells of the skin would also be killed which would be detrimental to the health of the patient.

Firstly, please note that Roizman et al. (U.S. Patent No. 6,340,673) is the primary reference in the above 103(a) rejection. Roizman et al. teach explicitly using an HSV-1 virus with a mutation in the γ34.5 gene to treat cancer and tumorigenic diseases both in the CNS and in all other parts of the body in a mammal including human, not necessarily limited to tumors of the CNS (see col. 5, lines 63-66; col. 9, lines 50-61; and the claims). Roizman et al. further teach direct injection of the virus into the tumor or intratumorally. Moreover, allowed claim 1 reads "A method of treating tumorigenic disease in a mammal comprising the step of administering at or near a site of a tumor of said tumorigenic disease a herpes simplex virus lacking an expressible γ_1 34.5 gene, whereby the growth of said tumor is suppressed". Thus, it is clear that the teachings of Roizman et al. are enabled. It should also be noted that claims of an issued U.S. Patent is presumed to be valid and that the enabled scope of an issued U.S. Patent is not limited by the exemplification. However, Roizman et al. do not specifically teach a method for treating a non-neuronal cancer in a mammal using the mutant herpes simplex virus strain 1716.

Secondly, Randazzo et al. already teach that the neuroattenuated HSV-1716 mutant that has a 759-bp deletion in γ34.5 is capable of lysing various murine melanoma cells *in vitro* (Table 1; page 99, left-handed column, first paragraph), and that the neuroattenuated HSV-1 mutant 1716 is at least a safe and effective therapeutic agent for intracranial melanoma.

Thirdly, please note that the present claims do not limit to any particular melanoma cell types that are resistant to lysis by HSV-1 mutant 1716. Moreover, it is

also clear from the teachings of the issued US Patent 6,340,673 that any herpes simplex virus lacking an expressible γ_1 34.5 gene is also capable of suppressing tumor growth in any tumorigenic disease in both in the CNS as well as in all other parts of the body in a mammal including human, and not necessarily limited to tumors of the CNS. Therefore, an ordinary skilled artisan would have a reasonable expectation of success to carry out the above modification in light of the teachings of Roizman et al. and Randazzo et al., at least by killing non-neuronal tumor cells in a mammal via the intratumoral injection route. The issue of "a safe and effective treatment" for the treated patient (e.g., healthy dividing cells of the skin would not be killed which would be detrimental to the health of the patient) is the domain of the Food and Drug Administration, and not of the USPTO.

Accordingly, claims 33 and 37-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Roizman et al. in view of Randazzo et al. for the same reasons already set forth in the Office Action mailed on 6/23/04 (pages 2-5).

Claims 33 and 40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Roizman et al. (U.S. Patent No. 6,340,673; Cited previously) in view of Randazzo et al. (Virology 211:94-101, 1995; IDS) as applied to claims 33, 37-40 above, and further in view of Martuza et al. (U.S. 6,139,834; Cited previously) for the same reasons already set forth in the Office Action mailed on 6/23/04 (pages 5-6).

Response to Arguments

Applicant's arguments related to the above rejection in the Amendment filed on 9/27/04 (pages 6-8) have been fully considered, but they are respectfully not found persuasive.

Applicants mainly argue that that the combination of the Randazzo paper and US Patent 6,340,673 (Roizman) to render claim 33 obvious is not possible for the reasons already set forth above, and therefore further combination with US Patent 6,139,834 (Martuza) to render claim 40 which is dependent on claim 33 is also inappropriate. Applicants further argue that the list of tumor types in Martuza is speculative because the examples in Martuza are concerned with neuronal tumor, and that any teaching of tumor types which can be treated in Martuza must take into account the overall teaching of Martuza, which is that a double mutated herpes simplex virus (mutations in the γ34.5 gene and the ribonucleotide reductase gene) is required.

Firstly, claim 30 is obvious from the combined teachings of Roizman et al. in view of Randazzo et al. for the reasons already discussed in the above response to Applicants' arguments for claims 33 and 37-40.

Secondly, with respect to Applicants' doubt on the enabled teachings of Martuza et al. (US Patent 6,139,834) once again please note that claims of an issued U.S. Patent is presumed to be valid and that the enabled scope of an issued U.S. Patent is not limited by the exemplification.

Thirdly, the killing of non-neuronal cancers such as mesothelioma, ovarian carcinoma and bladder cancer is not dependent on the extra mutation in the

ribonucleotide reductase gene. Particularly, Roizman (US Patent 6,340,673), **the primary reference**, already teaches that any herpes simplex virus lacking an expressible γ_1 34.5 gene is also capable of suppressing tumor growth in any tumorigenic disease in both in the CNS as well as in all other parts of the body in a mammal including human, and not necessarily limited to tumors of the CNS.

Accordingly, the rejection of claims 33 and 40 is maintained for the same reasons already set forth in the Office Action mailed on 6/23/04 (pages 5-6).

Conclusion

No claims are allowable.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Quang Nguyen, Ph.D., whose telephone number is (571) 272-0776.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's mentor, David Guzo, Ph.D., may be reached at (571) 272-0767, or SPE, Irem Yucel, Ph.D., at (571) 272-0781.

To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1636; Central Fax No. (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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Quang Nguyen, Ph.D.